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=> s paps synthetase and (dna or rna or nucleic acid)
   2 FILES SEARCHED...
L1          37 PAPS SYNTHETASE AND (DNA OR RNA OR NUCLEIC ACID)

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=> dup rem l1
PROCESSING COMPLETED FOR L1
L2           20 DUP REM L1 (17 DUPLICATES REMOVED)

=> s l2 and human
L3          15 L2 AND HUMAN

=> d l3 ibib ab 1-15

L3   ANSWER 1 OF 15     MEDLINE
ACCESSION NUMBER:   2003256125     MEDLINE
DOCUMENT NUMBER:    22664512   PubMed ID: 12781330
TITLE:              Pharmacogenetics of human 3'-phosphoadenosine
                    5'-phosphosulfate synthetase 1 (PAPSS1): gene resequencing,
                    sequence variation, and functional genomics.
AUTHOR:             Xu Zhen-Hua; Thomae Bianca A; Eckloff Bruce W; Wieben Eric
                    D; Weinshilboum Richard M
CORPORATE SOURCE:   Department of Molecular Pharmacology and Experimental
                    Therapeutics, Mayo Medical School-Mayo Clinic-Mayo
                    Foundation, Rochester, MN 55905, USA.
CONTRACT NUMBER:    R01 GM28157 (NIGMS)
     R01 GM35720 (NIGMS)
     UO1 GM61388 (NIGMS)
SOURCE:             BIOCHEMICAL PHARMACOLOGY, (2003 Jun 1) 65 (11) 1787-96.
                    Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200307
ENTRY DATE:         Entered STN: 20030604
                    Last Updated on STN: 20030709
                    Entered Medline: 20030708
AB   3'-Phosphoadenosine 5'-phosphosulfate (PAPS) is the high-energy "sulfate
     donor" for reactions catalyzed by sulfotransferase (SULT) enzymes.  The
     strict requirement of SULTs for PAPS suggests that PAPS synthesis might
     influence the rate of sulfate conjugation.  In humans, PAPS is synthesized
     from ATP and SO(4)(2-) by two isoforms of PAPS
```

synthetase (PAPSS): PAPSS1 and PAPSS2. As a step toward pharmacogenetic studies, we have resequenced the entire coding sequence of the **human** PAPSS1 gene, including exon-intron splice junctions, using **DNA** samples from 60 Caucasian-American and 58 African-American subjects. Twenty-one genetic polymorphisms were observed-1 insertion-deletion event and 20 single nucleotide polymorphisms (SNPs)-including two non-synonymous coding SNPs (cSNPs) that altered the following amino acids: Arg333Cys and Glu531Gln. Twelve pairs of these polymorphisms were tightly linked, and a total of twelve unequivocal haplotypes could be identified-two that were common to both ethnic groups and ten that were ethnic-specific. The Arg333Cys polymorphism, with an allele frequency of 2.5%, was observed only in **DNA** samples from Caucasian subjects. The Glu531Gln polymorphism was rare, with only a single copy of that allele in a **DNA** sample from an African-American subject. Transient expression in mammalian cells showed that neither of the non-synonymous cSNPs resulted in a change in the basal level of enzyme activity measured under optimal assay conditions. However, the Glu531Gln polymorphism altered the substrate kinetic properties of the enzyme. The Gln531 variant allozyme had a 5-fold higher K(m) value for SO(4)(2-) than did the wild-type allozyme and displayed monophasic kinetics for Na(2)SO(4). The wild-type allozyme (Glu531) showed biphasic kinetics for that substrate. These observations represent a step toward testing the hypothesis that genetic variation in PAPS synthesis catalyzed by PAPSS1 might alter in vivo sulfate conjugation.

L3 ANSWER 2 OF 15 MEDLINE
ACCESSION NUMBER: 2002199115 MEDLINE
DOCUMENT NUMBER: 21929363 PubMed ID: 11931653
TITLE: Transcriptional regulation of **human** 3'-phosphoadenosine 5'-phosphosulphate synthase 2.
AUTHOR: Shimizu Chikara; Fuda Hirotoshi; Lee Young C; Strott Charles A
CORPORATE SOURCE: Section on Steroid Regulation, Endocrinology and Reproduction Research Branch, National Institute of Child Health and Human Development, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20892-4510, U.S.A.
SOURCE: BIOCHEMICAL JOURNAL, (2002 Apr 15) 363 (Pt 2) 263-71. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020405
Last Updated on STN: 20020517
Entered Medline: 20020516

AB Sulphonation is a fundamental process that is essential for normal growth and development as well as maintenance of the internal milieu. The universal sulphonate donor molecule essential for all sulphoconjugation reactions is adenosine 3'-phosphate 5'-phosphosulphate (PAPS), which is produced from ATP and inorganic sulphate by the action of bifunctional PAPS synthase. There are two isozymes encoded by genes located on chromosome 4 (PAPS synthase 1) and chromosome 10 (PAPS synthase 2). The promoter for PAPS synthase 2 contains neither a TATAAA nor a CCAAT box, although a consensus initiator motif is present. Three **human** cell lines were used to examine promoter activity after transfection with various lengths of the 5'-flanking region of the PAPS synthase 2 gene fused to a reporter gene. Proximal promoter activity was located between bp -84 and bp -124 upstream of the purported transcription start site. This region contains two GC/GT boxes that are essential for full promoter activity, as indicated by deletion analysis and supported further by mutagenesis. A nuclear extract of SW13 cells, which highly express PAPS synthase 2, contained proteins that bound to probes possessing promoter-specific GC/GT boxes. Furthermore, the presence of specificity

protein (Sp) 1, Sp2 and Sp3 proteins in the nuclear extract was confirmed by supershift analysis. Co-transfection experiments using SL2 cells yielded additional support for the involvement of Sp1 in transcriptional regulation of the PAPS synthase 2 gene; the involvement of Sp2 and/or Sp3 remains to be clarified further.

L3 ANSWER 3 OF 15 MEDLINE
ACCESSION NUMBER: 2002051595 MEDLINE
DOCUMENT NUMBER: 21635880 PubMed ID: 11773860
TITLE: **Human** 3'-phosphoadenosine 5'-phosphosulfate synthetase 2 (PAPSS2) pharmacogenetics: gene resequencing, genetic polymorphisms and functional characterization of variant allozymes.
AUTHOR: Xu Zhen-Hua; Freimuth Robert R; Eckloff Bruce; Wieben Eric; Weinshilboum Richard M
CORPORATE SOURCE: Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Medical School-Mayo Clinic-Mayo Foundation, Rochester, MN 55905, USA.
CONTRACT NUMBER: RO1 GM28157 (NIGMS)
RO1 GM35720 (NIGMS)
UO1 GM61388 (NIGMS)
SOURCE: PHARMACOGENETICS, (2002 Jan) 12 (1) 11-21.
Journal code: 9211735. ISSN: 0960-314X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020326
Entered Medline: 20020325

AB 3'-Phosphoadenosine 5'-phosphosulfate (PAPS) is the sulfate donor cosubstrate for all sulfotransferase (SULT) enzymes. SULTs catalyze the sulfate conjugation of many endogenous and exogenous compounds, including drugs and other xenobiotics. In humans, PAPS is synthesized from adenosine 5'-triphosphate (ATP) and inorganic sulfate (SO2-4) by two isoforms, PAPSS1 and PAPSS2. Rare mutations that inactivate PAPSS2 are associated with **human** spondyloepimetaphyseal dysplasia and murine brachymorphism. To determine whether more common genetic polymorphisms that do not completely inactivate the enzyme might be one factor responsible for individual differences in sulfate conjugation, we previously cloned the **human** PAPSS2 gene. In the present studies, we 'resequenced' all twelve PAPSS2 exons and splice junctions, as well as approximately 500 bp of the 5'-flanking region, using 90 Polymorphism Discovery Resource (PDR) **DNA** samples from the Coriell Cell Repository. Twenty-two single nucleotide polymorphisms (SNPs) were observed, including four nonsynonymous coding region SNPs (cSNPs) that altered the following amino acids: Glu10Lys, Met281Leu,Val291Met and Arg432Lys. We also observed four insertions/deletions, including one sample that was homozygous for an 81-bp deletion in the 5'-flanking region 286 bp upstream from the site of transcription initiation. Transient expression studies showed that two of the nonsynonymous cSNPS, those that resulted in Glu10Lys and Val291Met alterations in encoded amino acids, showed significant decreases in levels of PAPSS activity. In the case of Glu10Lys, decreased activity was paralleled by a decrease in immunoreactive protein, while the Val291Met allozyme displayed a significant decrease in affinity for both ATP and Na2SO4 when compared to 'wild-type' enzyme, but without a significant alteration in level of immunoreactive protein. It will now be possible to test the hypothesis that these common, functionally significant PAPSS2 genetic polymorphisms might contribute to variations in sulfate conjugation in vivo.

L3 ANSWER 4 OF 15 MEDLINE
ACCESSION NUMBER: 2001522976 MEDLINE

DOCUMENT NUMBER: 21455682 PubMed ID: 11571655
TITLE: Conserved synteny between the Fugu and **human** PTEN locus and the evolutionary conservation of vertebrate PTEN function.
AUTHOR: Yu W P; Pallen C J; Tay A; Jirik F R; Brenner S; Tan Y H; Venkatesh B
CORPORATE SOURCE: Institute of Molecular and Cell Biology, 30 Medical Drive, Singapore 117609, Republic of Singapore.
SOURCE: ONCOGENE, (2001 Sep 6) 20 (39) 5554-61.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF325922
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010926
Last Updated on STN: 20011015
Entered Medline: 20011011

AB Mutations of PTEN, which encodes a protein-tyrosine and lipid phosphatase, are prevalent in a variety of **human** cancers. The **human** genome 'draft' sequence still lacks organization and much of the PTEN and adjacent loci remain undefined. The pufferfish, Fugu rubripes, by virtue of having a compact genome represents an excellent template for rapid vertebrate gene discovery. Sequencing of 56 kb from the Fugu pten (fpten) locus identified four complete genes and one partial gene homologous to **human** genes. Genes neighboring fpten include a PAPS synthase (fpapss2) differentially expressed between non-metastatic/metastatic **human** carcinoma cell lines, an inositol phosphatase (fminpp1) and an omega class glutathione-S-transferase (fgsto). We have determined the order of **human** BAC clones at the hPTEN locus and that the locus contains hPAPSS2 and hMINPP1 genes oriented as are their Fugu orthologs. Although the **human** genes span 500 kb, the Fugu genes lie within only 22 kb due to the compressed intronic and intergenic regions that typify this genome. Interestingly, and providing striking evidence of regulatory element conservation between widely divergent vertebrate species, the compact 2.1 kb fpten promoter is active in **human** cells. Also, like hPTEN, fpten has a growth and tumor suppressor activity in **human** glioblastoma cells, demonstrating conservation of protein function.

L3 ANSWER 5 OF 15 MEDLINE
ACCESSION NUMBER: 2001511193 MEDLINE
DOCUMENT NUMBER: 21442636 PubMed ID: 11558903
TITLE: Identification of sequence polymorphisms in two sulfation-related genes, PAPSS2 and SLC26A2, and an association analysis with knee osteoarthritis.
AUTHOR: Ikeda T; Mabuchi A; Fukuda A; Hiraoka H; Kawakami A; Yamamoto S; Machida H; Takatori Y; Kawaguchi H; Nakamura K; Ikegawa S
CORPORATE SOURCE: SNP Research Center, RIKEN (The Institute of Physical and Chemical Research, University of Tokyo, Japan.
SOURCE: JOURNAL OF HUMAN GENETICS, (2001) 46 (9) 538-43.
Journal code: 9808008. ISSN: 1434-5161.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010918
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Osteoarthritis (OA) is one of the most common musculoskeletal disorders and is characterized by degeneration of articular cartilage. Sulfation of extracellular matrix proteins in articular cartilage is an important step

in maintaining normal cartilage metabolism. Two sulfation-related genes have been reported as the causal genes of severe chondrodysplasias: mutations in PAPSS2 (3'-phosphoadenosine 5'-phosphosulfate synthase 2) cause spondylo-epimetaphyseal dysplasia (SEMD), and mutations in SLC26A2 (solute carrier family 26, member 2) cause diastrophic dysplasia. Given their critical roles in cartilage metabolism and the severe phenotypes that result from mutations in these genes, we examined PAPSS2 and SLC26A2 as candidate susceptibility loci for OA. We identified sequence polymorphisms in the coding and core promoter regions of these genes and analyzed their potential association with knee OA within the Japanese population. Ten sequence polymorphisms were detected in PAPSS2 and five in SLC26A2. An association analysis showed suggestive association of one minor polymorphism in the promoter region of SLC26A2. This 4-bp adenine deletion allele, del4A, was over-represented in knee OA ($P = 0.043$, odds ratio = 3.43) and is thought to confer a minor susceptibility to knee OA within the Japanese population. Haplotype analysis showed no evidence of association with the two genes, however, excluding them as major susceptibility loci for knee OA.

L3 ANSWER 6 OF 15 MEDLINE
ACCESSION NUMBER: 2001329633 MEDLINE
DOCUMENT NUMBER: 21290674 PubMed ID: 11396968
TITLE: Transcriptional regulation of **human** 3'-phosphoadenosine 5'-phosphosulfate synthase 1.
AUTHOR: Shimizu C; Fuda H; Lee Y C; Strott C A
CORPORATE SOURCE: Section on Steroid Regulation, Endocrinology and Reproduction Research Branch, NICHD, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Jun 15) 284 (3) 763-70.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

AB Sulfonation, which is essential for normal growth, development and maintenance of the internal milieu, requires the universal sulfonate donor molecule 3'-phosphoadenosine 5'-phosphosulfate (PAPS) produced from ATP and inorganic sulfate by two bifunctional PAPS synthase isozymes. The gene for PAPS synthase 1 containing neither a TATA nor a CCAAT box was found to be under the influence of the Sp1 family of transcription factors. Multiple GC/GT boxes are present in the proximal promoter region and deletion analysis implicated their involvement in transcription, a finding supported by mutational analysis of specific GC/GT boxes. Nuclear extract of SW13 cells, which highly express PAPS synthase 1, contains proteins that bind to probes possessing specific GC/GT boxes; furthermore, the presence of Sp1, Sp2, and Sp3 proteins in nuclear extracts was confirmed by supershift analysis. Cotransfection experiments using SL2 cells yielded additional support for the involvement of Sp1 in transcriptional regulation of the PAPS synthase 1 gene; the involvement of Sp2 and/or Sp3 is presently unclear.

L3 ANSWER 7 OF 15 MEDLINE
ACCESSION NUMBER: 2000026854 MEDLINE
DOCUMENT NUMBER: 20026854 PubMed ID: 10559207
TITLE: Genomic organization of the mouse and **human** genes encoding the ATP sulfurylase/adenosine 5'-phosphosulfate kinase isoform SK2.
AUTHOR: Kurima K; Singh B; Schwartz N B
CORPORATE SOURCE: Department of Pediatrics, University of Chicago, Chicago, Illinois 60637, USA.

CONTRACT NUMBER: AR-19622 (NIAMS)
HD-17332 (NICHD)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Nov 19) 274 (47) 33306-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF172857; GENBANK-AF172858; GENBANK-AF172859; GENBANK-AF172860; GENBANK-AF172861; GENBANK-AF172862; GENBANK-AF172863; GENBANK-AF172864; GENBANK-AF172865; GENBANK-AF172866; GENBANK-AF173361; GENBANK-AF173362; GENBANK-AF173363; GENBANK-AF173364; GENBANK-AF173365
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991214

AB Mammalian ATP sulfurylase/adenosine 5'-phosphosulfate (APS) kinase consists of kinase and sulfurylase domains, and catalyzes two sequential reactions to synthesize the universal sulfate donor, phosphoadenosine phosphosulfate (PAPS). In simpler organisms, the ATP sulfurylase and APS kinase reactions are catalyzed by separate enzymes encoded by two or three genes, suggesting that a fusion of separate genes during the course of evolution generated the bifunctional enzyme. We have characterized the genomic structure of the **PAPS synthetase** SK2 isoform genes for mouse (MSK2) and **human** (HSK2) and analyzed the possible fusion region. The MSK2 and HSK2 genes exhibit a common structure of 13 exons, including a 15-nucleotide alternatively spliced exon 8. Enzyme activities of several bacterially expressed exon assemblages showed exons 1-6 encode APS kinase, while exons 6-13 encode ATP sulfurylase. The MSK2 construct without the exon 6-encoded peptide showed no kinase or sulfurylase activity, demonstrating that exon 6 encodes sequences required for both activities. Exon 1 and its 5'-flanking sequence are highly divergent between the two species, and intron 1 of the HSK2 gene contains a region similar to the MSK2 promoter sequence, suggesting that it may be the remnant of a now-superceded regulatory region. The HSK2 promoter contains a GC-rich region, not present in the mouse promoter, and has few transcription factor binding sites in common with MSK2. These differences in the two promoter regions suggest that species-specific mechanisms regulate expression of the SK2 isoform.

L3 ANSWER 8 OF 15 MEDLINE
ACCESSION NUMBER: 1998236023 MEDLINE
DOCUMENT NUMBER: 98236023 PubMed ID: 9576487
TITLE: Sulfation in high endothelial venules: cloning and expression of the **human PAPS synthetase**.
AUTHOR: Girard J P; Baekkevold E S; Amalric F
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire Eucaryote du CNRS, Toulouse, France.. girard@ibcg.biotoul.fr
SOURCE: FASEB JOURNAL, (1998 May) 12 (7) 603-12.
Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y10387
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980521

AB High endothelial venules (HEVs) are specialized postcapillary venules found in lymphoid organs and chronically inflamed tissues that support

high levels of lymphocyte extravasation from the blood. Studies with chlorate, a metabolic inhibitor of sulfation, had previously revealed that production of PAPS (3'-phosphoadenosine-5'-phosphosulfate), the high-energy donor of sulfate, is required for sulfation and high-affinity recognition of HEV sialomucins GlyCAM-1 and CD34 by the lymphocyte homing receptor L-selectin. Here, we report the molecular characterization of a novel 2.5 kb **human** cDNA from MECA-79+ HEV-derived endothelial cells that encodes the target of chlorate, **PAPS synthetase**, a multifunctional enzyme containing domains for both ATP sulfurylase and adenosine-5'-phosphosulfate kinase. Functional expression of the isolated cDNA in Chinese hamster ovary cells results in high levels of PAPS synthesis, which is abolished by treatment of the transfected cells with chlorate. Northern blot analysis reveals a wide tissue distribution of **PAPS synthetase** mRNA in the **human** body, suggesting that **human PAPS synthetase** may be important for sulfation not only of HEV sialomucins, but also of many other molecules, including mucins such as the P-selectin ligand PSGL-1, proteoglycans, hormones, neurotransmitters, drugs, and xenobiotics.

L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:777664 CAPLUS
DOCUMENT NUMBER: 137:277250
TITLE: Differentially-expressed and up-regulated polynucleotides and polypeptides in breast cancer and their diagnostic and therapeutic uses
INVENTOR(S): Sun, Zairen; Jay, Gilbert
PATENT ASSIGNEE(S): Origene Technologies, Inc, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078642	A2	20021010	WO 2002-US9990	20020401

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-279678P P 20010330
US 2001-293218P P 20010525

AB The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clin. medicine, forensic, etc. The 269 **human** polynucleotides are differentially expressed in cancers, esp. breast cancers, and are therefore are useful in variety of ways, including, but not limited to, as mol. markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, detg. predisposition to, etc., diseases and conditions, such as cancer and other cell-cycle diseases, esp. relating to breast. The identification of specific genes, and groups of genes, expressed in a pathway physiol. relevant to cancer permits the definition of disease pathways and the delineation of targets in these pathways which are useful in diagnostic, therapeutic, and clin. applications.

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:616256 CAPLUS
DOCUMENT NUMBER: 137:181594
TITLE: Dominant-negative variants of **human** protein kinases that inhibit the phosphorylation activity of their active enzyme isoforms
INVENTOR(S): Levine, Zurit; Bernstein, Jeanne
PATENT ASSIGNEE(S): Compugen Ltd., Israel
SOURCE: U.S. Pat. Appl. Publ., 170 pp., Cont.-in-part of U.S. Ser. No. 724,676.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002110811	A1	20020815	US 2001-771161	20010126

PRIORITY APPLN. INFO.:
IL 2000-135619 A 20000512
IL 2000-136776 A 20000615
US 2000-724676 A2 20001128

AB The present invention concerns 91 **nucleic acid** sequences and amino acid sequences of variants of various **human** kinases, i.e. of sequences which inhibit activity of kinases in a dominant manner. The variants lack a domain or region required for phosphorylation, and thus may be dominant-neg. kinases obtained by alternative splicing of known original sequences of the kinase genes. The novel dominant-neg. kinase variants of the invention are not merely artificially truncated forms, fragments or mutations of known genes, but rather novel sequences which naturally occur within the body of individuals. The invention also concerns pharmaceutical compns. and detection methods using these sequences.

L3 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:320060 CAPLUS
DOCUMENT NUMBER: 134:339179
TITLE: Nucleic acids and proteins associated with cancer as antitumor targets
INVENTOR(S): Burmer, Glenna C.; Brown, Joseph P.; Pritchard, David
PATENT ASSIGNEE(S): Lifespan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030964	A2	20010503	WO 2000-US29126	20001020
WO 2001030964	A3	20010809		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001013397	A5	20010508	AU 2001-13397	20001020

PRIORITY APPLN. INFO.:
US 1999-161232P P 19991022
US 2000-693783 A 20001019
WO 2000-US29126 W 20001020

AB This invention relates to the discovery of nucleic acids assocd. with cell proliferation, neoplasia, cell transformation, malignant tumor formation and metastasis and uses therefor. The present invention provides a method for cancer diagnosing by detecting the overexpression or the underexpression of a cancer-assocd. mRNA in the tissue of interest, preferably in liver, breast, prostate, kidney and colon. In another aspect, the invention provides methods for arresting cancer and a method for identifying a modulators of cancer development.

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:115030 CAPLUS
DOCUMENT NUMBER: 132:275908
TITLE: **Human** 3'-Phosphoadenosine 5'-Phosphosulfate Synthetase 1 (PAPSS1) and PAPSS2: Gene Cloning, Characterization and Chromosomal Localization
AUTHOR(S): Xu, Zhen-Hua; Otterness, Diane M.; Freimuth, Robert R.; Carlini, Edward J.; Wood, Thomas C.; Mitchell, Steve; Moon, Eunpyo; Kim, Ung-Jin; Xu, Jing-Ping; Siciliano, Michael J.; Weinshilboum, Richard M.
CORPORATE SOURCE: Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Medical School/Mayo Graduate School/Mayo Clinic, Rochester, MN, 55905, USA
SOURCE: Biochemical and Biophysical Research Communications (2000), 268(2), 437-444
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sulfate conjugation is an important pathway in the metab. of a large no. of exogenous and endogenous compds. These reactions are catalyzed by sulfotransferase (SULT) enzymes that utilize 3'-phosphoadenosine 5'-phosphosulfate (PAPS) as a sulfate donor. PAPS is synthesized from ATP and inorg. sulfate by **PAPS synthetase** (PAPSS). Two sep. PAPSS cDNAs, PAPSS1 and PAPSS2, have been identified in **human** tissues. We have cloned and characterized the genes for **human** PAPSS1 and PAPSS2 to make it possible to study the pharmacogenomics of these enzymes. Both genes consisted of 12 exons with virtually identical exon-intron splice junction locations. All splice junctions conformed to the "GT-AG" rule. The total length of PAPSS1 was approx. 108 kb, while that of PAPSS2 was greater than 37 kb. The 5'-flanking region of PAPSS1 did not include a TATA box sequence near the site of transcription initiation, but PAPSS2 had a TATA motif located 21 bp upstream from the site of transcription initiation. Northern blot anal. showed that the major PAPSS1 and PAPSS2 transcripts were approx. 2.7 and 4.2 kb in length, resp. PAPSS1 mapped to **human** chromosome band 4q24 while PAPSS2 mapped to 10q22-23 by fluorescence in situ hybridization anal. Cloning and structural characterization of PAPSS1 and PAPSS2 will make it possible to perform mol. genetic and pharmacogenomic studies of these important enzymes in humans. (c) 2000 Academic Press.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:368932 BIOSIS
DOCUMENT NUMBER: PREV200200368932
TITLE: Tissue distribution and functional analysis of the bifunctional ATP sulfurylase/APS kinase family in mouse.
AUTHOR(S): Cortes, Mauricio (1); Singh, Bhawani; Kurima, Kiyoto; Deyrup, Andrea; Schwartz, N. B.
CORPORATE SOURCE: (1) Biochemistry and Molecular Biology, University of Chicago, 5841 S.Maryland Ave, M.C 5058, Chicago, IL, 60637 USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A551. http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of the Professional Research

Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Sulfation, an important post-translational modification of numerous molecules requires the synthesis of the high-energy sulfate donor, phosphoadenosine-phosphosulfate (PAPS). In higher organisms, the synthesis of PAPS is catalyzed by a single bifunctional enzyme, **PAPS synthetase** (SK). We have identified a gene family encoding two SK isoforms in mouse and **human**. Northern blot analysis and in situ hybridization studies, and immunohistochemical localization using isoform specific antibodies have demonstrated different tissue expression of the two isoforms. SK1 is predominantly expressed in the brain, and kidney while SK2 is predominantly expressed in cartilage. In vitro activity assays of each isoform show comparable distribution pattern. The functional similarity and unique tissue specificity of these two isoforms suggests non-redundant roles and that different regulatory elements may control the temporal and spatial expression of SK isoforms critical for normal development.

L3 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:363670 BIOSIS
DOCUMENT NUMBER: PREV200100363670
TITLE: Preparation of highly pure 3'-phosphoadenosine-5'-phosphosulfate (PAPS) using recombinant **human PAPS synthetase** and purification by ion exchange high performance liquid chromatography.
AUTHOR(S): Muckel, E. (1); Landsiedel, R. (1); Glatt, H. R. (1)
CORPORATE SOURCE: (1) German Institute for human Nutrition, Arthur-Scheunert-Allee 114-116, 14558, Bergholz-Rehbruecke Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (2001) Vol. 363, No. 4 Supplement , pp. R137. print.
Meeting Info.: 42nd Spring Meeting of the German Society for Experimental and Cllinical Pharmacology and Toxicology Mainz, Germany March 13-15, 2001
ISSN: 0028-1298.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:311342 BIOSIS
DOCUMENT NUMBER: PREV199900311342
TITLE: Molecular cloning of a novel **human PAPS synthetase** which is differentially expressed in metastatic and non-metastatic colon carcinoma cells.
AUTHOR(S): Franzon, Vicki L.; Gibson, Mark A.; Hatzinikolas, George; Woollatt, Erica; Sutherland, Grant R.; Cleary, Edward G. (1)
CORPORATE SOURCE: (1) Department of Pathology, University of Adelaide, Adelaide, SA, 5005 Australia
SOURCE: International Journal of Biochemistry & Cell Biology, (May, 1999) Vol. 31, No. 5, pp. 613-626.
ISSN: 1357-2725.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Subtractive hybridisation was used to select for genes which are differentially expressed between a highly metastatic **human** colon carcinoma cell line, KM12SM, and the isogenetic non-metastatic cell line, KM12C. This led to the isolation of cDNA clones for a novel **human** adenosine 5'-phosphosulphate kinase/ATP sulphurylase (**PAPS synthetase**). Northern hybridisation revealed a single 4.2 kb mRNA

species which showed an approximately 20-fold higher level of expression in the non-metastatic cell line than in the metastatic cell line. The overlapping cDNA clones together covered 3,774 bp including the entire coding region of 1,842 bp encoding a protein of 614 amino acids (calculated molecular mass of 69,496 Da). The protein contains consensus sequences for APS kinase and ATP sulphurylase, in its amino- and carboxy-terminal regions, respectively, as well as other sequences that are highly conserved amongst ATP sulphurylases and APS kinases. Interestingly, consensus sequences for GTPase activity were also identified, indicating that enzyme activity may be regulated by an intrinsic GTPase mechanism. Overall the new protein is 78% homologous with a previously described **human PAPS synthetase** (PAPSS1) indicating that we have identified the second member of a gene family which we have provisionally named PAPSS2. The gene locus for PAPSS2 was identified on chromosome 10 at 10q23.1-q23.2. This locus has synteny with the mouse brachymorphic gene recently identified as a **PAPS synthetase** (SK2). PAPSS2 appears to be the **human** homologue of this gene and thus PAPSS2 is likely to be important in **human** skeletogenesis.

=> s l2 and mouse
L4 4 L2 AND MOUSE

=> d l4 1-4 ibib ab

L4 ANSWER 1 OF 4 MEDLINE
ACCESSION NUMBER: 2000026854 MEDLINE
DOCUMENT NUMBER: 20026854 PubMed ID: 10559207
TITLE: Genomic organization of the **mouse** and human genes encoding the ATP sulfurylase/adenosine 5'-phosphosulfate kinase isoform SK2.
AUTHOR: Kurima K; Singh B; Schwartz N B
CORPORATE SOURCE: Department of Pediatrics, University of Chicago, Chicago, Illinois 60637, USA.
CONTRACT NUMBER: AR-19622 (NIAMS)
HD-17332 (NICHD)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Nov 19) 274 (47) 33306-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF172857; GENBANK-AF172858; GENBANK-AF172859; GENBANK-AF172860; GENBANK-AF172861; GENBANK-AF172862; GENBANK-AF172863; GENBANK-AF172864; GENBANK-AF172865; GENBANK-AF172866; GENBANK-AF173361; GENBANK-AF173362; GENBANK-AF173363; GENBANK-AF173364; GENBANK-AF173365
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991214

AB Mammalian ATP sulfurylase/adenosine 5'-phosphosulfate (APS) kinase consists of kinase and sulfurylase domains, and catalyzes two sequential reactions to synthesize the universal sulfate donor, phosphoadenosine phosphosulfate (PAPS). In simpler organisms, the ATP sulfurylase and APS kinase reactions are catalyzed by separate enzymes encoded by two or three genes, suggesting that a fusion of separate genes during the course of evolution generated the bifunctional enzyme. We have characterized the genomic structure of the **PAPS synthetase** SK2 isoform genes for **mouse** (MSK2) and human (HSK2) and analyzed the possible fusion region. The MSK2 and HSK2 genes exhibit a common structure of 13 exons, including a 15-nucleotide alternatively spliced exon 8. Enzyme activities of several bacterially expressed exon

assemblages showed exons 1-6 encode APS kinase, while exons 6-13 encode ATP sulfurylase. The MSK2 construct without the exon 6-encoded peptide showed no kinase or sulfurylase activity, demonstrating that exon 6 encodes sequences required for both activities. Exon 1 and its 5'-flanking sequence are highly divergent between the two species, and intron 1 of the HSK2 gene contains a region similar to the MSK2 promoter sequence, suggesting that it may be the remnant of a now-superceded regulatory region. The HSK2 promoter contains a GC-rich region, not present in the **mouse** promoter, and has few transcription factor binding sites in common with MSK2. These differences in the two promoter regions suggest that species-specific mechanisms regulate expression of the SK2 isoform.

L4 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:368932 BIOSIS
DOCUMENT NUMBER: PREV200200368932
TITLE: Tissue distribution and functional analysis of the bifunctional ATP sulfurylase/APS kinase family in **mouse**.
AUTHOR(S): Cortes, Mauricio (1); Singh, Bhawani; Kurima, Kiyoto; Deyrup, Andrea; Schwartz, N. B.
CORPORATE SOURCE: (1) Biochemistry and Molecular Biology, University of Chicago, 5841 S.Maryland Ave, M.C 5058, Chicago, IL, 60637 USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A551. http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Sulfation, an important post-translational modification of numerous molecules requires the synthesis of the high-energy sulfate donor, phosphoadenosine-phosphosulfate (PAPS). In higher organisms, the synthesis of PAPS is catalyzed by a single bifunctional enzyme, **PAPS synthetase** (SK). We have identified a gene family encoding two SK isoforms in **mouse** and human. Northern blot analysis and in situ hybridization studies, and immunohistochemical localization using isoform specific antibodies have demonstrated different tissue expression of the two isoforms. SK1 is predominantly expressed in the brain, and kidney while SK2 is predominantly expressed in cartilage. In vitro activity assays of each isoform show comparable distribution pattern. The functional similarity and unique tissue specificity of these two isoforms suggests non-redundant roles and that different regulatory elements may control the temporal and spatial expression of SK isoforms critical for normal development.

L4 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:311342 BIOSIS
DOCUMENT NUMBER: PREV199900311342
TITLE: Molecular cloning of a novel human **PAPS synthetase** which is differentially expressed in metastatic and non-metastatic colon carcinoma cells.
AUTHOR(S): Franzon, Vicki L.; Gibson, Mark A.; Hatzinikolas, George; Woollatt, Erica; Sutherland, Grant R.; Cleary, Edward G. (1)
CORPORATE SOURCE: (1) Department of Pathology, University of Adelaide, Adelaide, SA, 5005 Australia
SOURCE: International Journal of Biochemistry & Cell Biology, (May, 1999) Vol. 31, No. 5, pp. 613-626.
ISSN: 1357-2725.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Subtractive hybridisation was used to select for genes which are differentially expressed between a highly metastatic human colon carcinoma cell line, KM12SM, and the isogenetic non-metastatic cell line, KM12C. This led to the isolation of cDNA clones for a novel human adenosine 5'-phosphosulphate kinase/ATP sulphurylase (**PAPS synthetase**). Northern hybridisation revealed a single 4.2 kb mRNA species which showed an approximately 20-fold higher level of expression in the non-metastatic cell line than in the metastatic cell line. The overlapping cDNA clones together covered 3,774 bp including the entire coding region of 1,842 bp encoding a protein of 614 amino acids (calculated molecular mass of 69,496 Da). The protein contains consensus sequences for APS kinase and ATP sulphurylase, in its amino- and carboxy-terminal regions, respectively, as well as other sequences that are highly conserved amongst ATP sulphurylases and APS kinases. Interestingly, consensus sequences for GTPase activity were also identified, indicating that enzyme activity may be regulated by an intrinsic GTPase mechanism. Overall the new protein is 78% homologous with a previously described human **PAPS synthetase** (PAPSS1) indicating that we have identified the second member of a gene family which we have provisionally named PAPSS2. The gene locus for PAPSS2 was identified on chromosome 10 at 10q23.1-q23.2. This locus has synteny with the **mouse** brachymorphic gene recently identified as a **PAPS synthetase** (SK2). PAPSS2 appears to be the human homologue of this gene and thus PAPSS2 is likely to be important in human skeletogenesis.

L4 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003016481 EMBASE
TITLE: Identification and functional characterization of the novel BM-motif in the murine phosphoadenosine phosphosulfate (**PAPS**) **synthetase**.
AUTHOR: Singh B.; Schwartz N.B.
CORPORATE SOURCE: N.B. Schwartz, Dept. of Pediatrics, University of Chicago, MC 5058, 5841 S. Maryland Ave., Chicago, IL 60637, United States. n-schwartz@uchicago.edu
SOURCE: Journal of Biological Chemistry, (3 Jan 2003) 278/1 (71-75).
Refs: 16
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **PAPS synthetase** (SK) catalyzes the two sequential reactions of phosphoadenosine phosphosulfate (PAPS) synthesis. A functional motif in the kinase domain of **mouse** SK, designated the BM-motif ((86) LDGDNhRxhh(N/S)(K/R)(97)), was defined in the course of identifying the brachymorphic (bm) defect. Sequence comparison and the secondary structure predicted for APS kinase suggest that the BM-motif consists of a DGD-turn sequence flanked by other conserved residues. Mutational analysis of the DGD-turn revealed that a flexible and neutral amino acid is preferred at residue 88, that negatively charged residues are strictly required at positions 87 and 89, and that the active site is rigid. The reduction in kinase activity for all DGD-turn mutants, except G88A, was much less severe than the reduction in overall activity, indicating that the BM-motif may also be playing a role in adenosine phosphosulfate (APS) channeling. Two switch mutations, LD86DL and DN89ND, designed to test the positional constraints of Asp(87) and Asp(89), exhibited complete loss of both kinase and overall activities, while LD86DL also exhibited a significant (60%) loss of reverse sulfurylase activity, suggesting that this peptide region is interacting with the sulfurylase domain as well as functioning in the kinase reaction. Other residues targeted for mutational analysis were the highly conserved flanking Asn(90), Arg(92), and Lys(97). N90A resulted in a partial (30%)

loss in kinase and overall activities, R92A exhibited total loss of kinase and overall activities, and K97A had no effect on any of the three activities. The complexity of the bifunctional SK in catalyzing the kinase reaction and channeling APS is illustrated by the strict requirements of this novel structural motif in the kinase active site.

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=> d his

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     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, EMBASE' ENTERED AT 14:48:36 ON
     15 JUL 2003

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, EMBASE' ENTERED AT 14:48:54 ON
     15 JUL 2003
L1            37 S PAPS SYNTHETASE AND (DNA OR RNA OR NUCLEIC ACID)
L2            20 DUP REM L1 (17 DUPLICATES REMOVED)
L3            15 S L2 AND HUMAN
L4             4 S L2 AND MOUSE

=> s l1 and 1990-1999/py
L5           16 L1 AND 1990-1999/PY

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6             6 DUP REM L5 (10 DUPLICATES REMOVED)

=> d l6 1-6 ibib ab

L6   ANSWER 1 OF 6     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:    2000026854     MEDLINE
DOCUMENT NUMBER:     20026854    PubMed ID: 10559207
TITLE:               Genomic organization of the mouse and human genes encoding
                     the ATP sulfurylase/adenosine 5'-phosphosulfate kinase
                     isoform SK2.
AUTHOR:              Kurima K; Singh B; Schwartz N B
CORPORATE SOURCE:    Department of Pediatrics, University of Chicago, Chicago,
                     Illinois 60637, USA.
CONTRACT NUMBER:     AR-19622 (NIAMS)
     HD-17332 (NICHD)
SOURCE:              JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Nov 19)
                     274 (47) 33306-12.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
OTHER SOURCE:        GENBANK-AF172857; GENBANK-AF172858; GENBANK-AF172859;
                     GENBANK-AF172860; GENBANK-AF172861; GENBANK-AF172862;
                     GENBANK-AF172863; GENBANK-AF172864; GENBANK-AF172865;
                     GENBANK-AF172866; GENBANK-AF173361; GENBANK-AF173362;
                     GENBANK-AF173363; GENBANK-AF173364; GENBANK-AF173365
ENTRY MONTH:         199912
ENTRY DATE:          Entered STN: 20000113
                     Last Updated on STN: 20000113
                     Entered Medline: 19991214
AB   Mammalian ATP sulfurylase/adenosine 5'-phosphosulfate (APS) kinase
     consists of kinase and sulfurylase domains, and catalyzes two sequential
     reactions to synthesize the universal sulfate donor, phosphoadenosine
     phosphosulfate (PAPS). In simpler organisms, the ATP sulfurylase and APS
     kinase reactions are catalyzed by separate enzymes encoded by two or three
     genes, suggesting that a fusion of separate genes during the course of
     evolution generated the bifunctional enzyme. We have characterized the
     genomic structure of the PAPS synthetase SK2 isoform
```

genes for mouse (MSK2) and human (HSK2) and analyzed the possible fusion region. The MSK2 and HSK2 genes exhibit a common structure of 13 exons, including a 15-nucleotide alternatively spliced exon 8. Enzyme activities of several bacterially expressed exon assemblages showed exons 1-6 encode APS kinase, while exons 6-13 encode ATP sulfurylase. The MSK2 construct without the exon 6-encoded peptide showed no kinase or sulfurylase activity, demonstrating that exon 6 encodes sequences required for both activities. Exon 1 and its 5'-flanking sequence are highly divergent between the two species, and intron 1 of the HSK2 gene contains a region similar to the MSK2 promoter sequence, suggesting that it may be the remnant of a now-superceded regulatory region. The HSK2 promoter contains a GC-rich region, not present in the mouse promoter, and has few transcription factor binding sites in common with MSK2. These differences in the two promoter regions suggest that species-specific mechanisms regulate expression of the SK2 isoform.

L6 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
ACCESSION NUMBER: 1999:236336 BIOSIS
DOCUMENT NUMBER: PREV199900236336
TITLE: Activity and stability of recombinant bifunctional rearranged and monofunctional domains of ATP-sulfurylase and adenosine 5'-phosphosulfate kinase.
AUTHOR(S): Deyrup, Andrea T.; Krishnan, Srinivasan; Singh, Bhawani; Schwartz, Nancy B. (1)
CORPORATE SOURCE: (1) Dept. of Pediatrics, University of Chicago, 5841 S. Maryland Ave., Chicago, IL, 60637 USA
SOURCE: Journal of Biological Chemistry, (**April 16, 1999**) Vol. 274, No. 16, pp. 10751-10757.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Murine adenosine 3'-phosphate 5'-phosphosulfate (**PAPS**) **synthetase** consists of a COOH-terminal ATP-sulfurylase domain covalently linked through a nonhomologous intervening sequence to an NH2-terminal adenosine 5'-phosphosulfate (APS) kinase domain forming a bifunctional fused protein. Possible advantages of bifunctionality were probed by separating the domains on the cDNA level and expressing them as monofunctional proteins. Expressed protein generated from the ATP-sulfurylase domain alone was fully active in both the forward and reverse sulfurylase assays. APS kinase-only recombinants exhibited no kinase activity. However, extension of the kinase domain at the COOH terminus by inclusion of the 36 residue linker region restored kinase activity. An equimolar mixture of the two monofunctional enzymes catalyzed the overall reaction (synthesis of PAPS from ATP + SO42-) comparably to the fused bifunctional enzyme. The importance of the domain order and organization was demonstrated by generation of a series of rearranged recombinants in which the order of the two active domains was reversed or altered relative to the linker region. The critical role of the linker region was established by generation of recombinants that had the linker deleted or rearranged relative to the two active domains. The intrinsic stability of the various recombinants was also investigated by measuring enzyme deactivation as a function of time of incubation at 25 or 37 degreeC. The expressed monofunctional ATP-sulfurylase, which was initially fully active, was unstable compared with the fused bifunctional wild type enzyme, decaying with a t1/2 of 10 min at 37 degreeC. Progressive extension by addition of kinase sequence at the NH2-terminal side of the sulfurylase recombinant eventually stabilized sulfurylase activity. Sulfurylase activity was significantly destabilized in a time-dependent manner in the rearranged proteins as well. In contrast, no significant deactivation of any truncated kinase-containing recombinants or misordered kinase recombinants was observed at either temperature. It would therefore appear that fusion of the two enzymes enhances the intrinsic stability of the sulfurylase only.

L6 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
ACCESSION NUMBER: 1999:311342 BIOSIS
DOCUMENT NUMBER: PREV199900311342
TITLE: Molecular cloning of a novel human **PAPS synthetase** which is differentially expressed in metastatic and non-metastatic colon carcinoma cells.
AUTHOR(S): Franzon, Vicki L.; Gibson, Mark A.; Hatzinikolas, George; Woollatt, Erica; Sutherland, Grant R.; Cleary, Edward G. (1)
CORPORATE SOURCE: (1) Department of Pathology, University of Adelaide, Adelaide, SA, 5005 Australia
SOURCE: International Journal of Biochemistry & Cell Biology, (**May, 1999**) Vol. 31, No. 5, pp. 613-626. ISSN: 1357-2725.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Subtractive hybridisation was used to select for genes which are differentially expressed between a highly metastatic human colon carcinoma cell line, KM12SM, and the isogenetic non-metastatic cell line, KM12C. This led to the isolation of cDNA clones for a novel human adenosine 5'-phosphosulphate kinase/ATP sulphurylase (**PAPS synthetase**). Northern hybridisation revealed a single 4.2 kb mRNA species which showed an approximately 20-fold higher level of expression in the non-metastatic cell line than in the metastatic cell line. The overlapping cDNA clones together covered 3,774 bp including the entire coding region of 1,842 bp encoding a protein of 614 amino acids (calculated molecular mass of 69,496 Da). The protein contains consensus sequences for APS kinase and ATP sulphurylase, in its amino- and carboxy-terminal regions, respectively, as well as other sequences that are highly conserved amongst ATP sulphurylases and APS kinases. Interestingly, consensus sequences for GTPase activity were also identified, indicating that enzyme activity may be regulated by an intrinsic GTPase mechanism. Overall the new protein is 78% homologous with a previously described human **PAPS synthetase** (PAPSS1) indicating that we have identified the second member of a gene family which we have provisionally named PAPSS2. The gene locus for PAPSS2 was identified on chromosome 10 at 10q23.1-q23.2. This locus has synteny with the mouse brachymorphic gene recently identified as a **PAPS synthetase** (SK2). PAPSS2 appears to be the human homologue of this gene and thus PAPSS2 is likely to be important in human skeletogenesis.

L6 ANSWER 4 OF 6 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998236023 MEDLINE
DOCUMENT NUMBER: 98236023 PubMed ID: 9576487
TITLE: Sulfation in high endothelial venules: cloning and expression of the human **PAPS synthetase**
AUTHOR: Girard J P; Baekkevold E S; Amalric F
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire Eucaryote du CNRS, Toulouse, France.. girard@ibcg.biotoul.fr
SOURCE: FASEB JOURNAL, **(1998 May)** 12 (7) 603-12. Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y10387
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980521
AB High endothelial venules (HEVs) are specialized postcapillary venules found in lymphoid organs and chronically inflamed tissues that support high levels of lymphocyte extravasation from the blood. Studies with

chlorate, a metabolic inhibitor of sulfation, had previously revealed that production of PAPS (3'-phosphoadenosine-5'-phosphosulfate), the high-energy donor of sulfate, is required for sulfation and high-affinity recognition of HEV sialomucins GlyCAM-1 and CD34 by the lymphocyte homing receptor L-selectin. Here, we report the molecular characterization of a novel 2.5 kb human cDNA from MECA-79+ HEV-derived endothelial cells that encodes the target of chlorate, **PAPS synthetase**, a multifunctional enzyme containing domains for both ATP sulfurylase and adenosine-5'-phosphosulfate kinase. Functional expression of the isolated cDNA in Chinese hamster ovary cells results in high levels of PAPS synthesis, which is abolished by treatment of the transfected cells with chlorate. Northern blot analysis reveals a wide tissue distribution of **PAPS synthetase** mRNA in the human body, suggesting that human **PAPS synthetase** may be important for sulfation not only of HEV sialomucins, but also of many other molecules, including mucins such as the P-selectin ligand PSGL-1, proteoglycans, hormones, neurotransmitters, drugs, and xenobiotics.

L6 ANSWER 5 OF 6 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998092112 MEDLINE
DOCUMENT NUMBER: 98092112 PubMed ID: 9431815
TITLE: cDNA sequence and expression pattern of the Drosophila melanogaster **PAPS synthetase** gene: a new salivary gland marker.
AUTHOR: Jullien D; Crozatier M; Kas E
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire Eucaryote, C.N.R.S. U.P.R. 9006, Toulouse, France.
SOURCE: MECHANISMS OF DEVELOPMENT, **(1997 Nov)** 68 (1-2) 179-86.
Journal code: 9101218. ISSN: 0925-4773.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Y12861
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980312
Last Updated on STN: 19990129
Entered Medline: 19980305

AB **PAPS synthetase** is a bifunctional enzyme containing both ATP sulfurylase and APS kinase activities required for the biosynthesis of PAPS, the sulfate donor in sulfation reactions. Here we report the sequence of the Drosophila melanogaster **PAPS synthetase**, the first gene implicated in the sulfation pathway to be described in that organism, and the characterization of its specificity of expression in embryos. Whole-mount in situ hybridization reveals that DmPAPSS is a novel salivary gland marker. At the end of embryogenesis, expression of DmPAPSS is also observed at the entry and exit of the gut and the posterior spiracles. We discuss the possibility that the pattern of expression of the DmPAPSS gene might reflect a major role for sulfation in mucus biosynthesis at the end of Drosophila embryogenesis.

L6 ANSWER 6 OF 6 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96096529 MEDLINE
DOCUMENT NUMBER: 96096529 PubMed ID: 8522184
TITLE: A multifunctional Urechis caupo protein, **PAPS synthetase**, has both ATP sulfurylase and APS kinase activities.
AUTHOR: Rosenthal E; Leustek T
CORPORATE SOURCE: Kewalo Marine Laboratory, University of Hawaii, Honolulu 96813, USA.
SOURCE: GENE, **(1995 Nov 20)** 165 (2) 243-8.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D33155; GENBANK-L39001; GENBANK-T09181
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960219
Last Updated on STN: 19960219
Entered Medline: 19960122

AB The synthesis of 3'-phosphoadenosine-5'-phosphosulfate (PAPS) from inorganic sulfate and ATP requires two enzymes, ATP sulfurylase (SUL) and adenosine-5'-phosphosulfate kinase (KIN). In bacteria, fungi, yeast and plants, the two enzymes are present on separate polypeptide chains. We have identified the first animal gene coding for these enzymes. In the marine worm, Urechis caupo (Uc), both SUL and KIN are present on a single polypeptide chain. This protein, which we call **PAPS synthetase** (PAPSS), is able to complement yeast mutants lacking either enzyme. The Uc PAPSS mRNA is present in oocytes, but is not translated until after fertilization. At least three adult tissues, gut, ceolomocytes and body wall, also contain the mRNA, but at lower concentrations than are found in embryos. Partial sequences of a similar gene from Caenorhabditis elegans (Ce) were detected in a search of the GenBank expressed sequence tag database. Comparison of these Uc and Ce PAPSS sequences with the sequences of cloned genes from non-animal organisms strongly suggests that the animal genes evolved through the fusion of the SUL- and KIN-encoding genes from lower organisms.

=> d his

(FILE 'HOME' ENTERED AT 14:47:45 ON 15 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, EMBASE' ENTERED AT 14:48:36 ON 15 JUL 2003

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, EMBASE' ENTERED AT 14:48:54 ON 15 JUL 2003

L1 37 S PAPS SYNTHETASE AND (DNA OR RNA OR NUCLEIC ACID)
L2 20 DUP REM L1 (17 DUPLICATES REMOVED)
L3 15 S L2 AND HUMAN
L4 4 S L2 AND MOUSE
L5 16 S L1 AND 1990-1999/PY
L6 6 DUP REM L5 (10 DUPLICATES REMOVED)

=> log
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	51.90	56.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.60	-2.60

STN INTERNATIONAL LOGOFF AT 14:56:31 ON 15 JUL 2003

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End of Result Set

☐ Generate Collection Print

L9: Entry 3 of 3 File: USPT May 1, 2001

US-PAT-NO: 6225100
DOCUMENT-IDENTIFIER: US 6225100 B1
**** See image for Certificate of Correction ****

TITLE: Arylsulfotransferase

DATE-ISSUED: May 1, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Maurina-Brunker; Julie	Appleton	WI		
Grund; Alan D.	Manitowoc	WI		

US-CL-CURRENT: 435/193; 435/183, 530/350

CLAIMS:

What is claimed is:

1. An isolated Clostridium arysulfotransferase comprising the following characteristics:

a. a total molecular weight of about 320 kD;

b. 4 subunits having a molecular weight of about 80 kD each;

c. an optimum pH for sulfation activity at about 8.2;

d. a specific activity of greater than about 15.0 units per milligram of protein;

e. an ability to maintain greater than about 40% activity for about 2 weeks when stored at 4.degree. C. without being immobilized or otherwise protected; and

f. an ability to use aryl sulfates selected from the group consisting of p-nitrophenylsulfate, p-acetylphenylsulfate, 4-methylumbelliferyl sulfate, estrone sulfate, p-nitrocatechol sulfate, phenolphthalein sulfate and indoxyl sulfate, as sulfate donors.

2. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase is a naturally occurring Clostridium innocuum arylsulfotransferase.

3. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase is isolated from Clostridium innocuum 554 ATCC 55803.

4. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase catalyzes the transfer of a sulfate group to cholecystokinin-8 with a yield of greater than about 35% within about 6 hours.

5. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase catalyzes the transfer of a sulfate group to cholecystokinin-8 with a yield of greater than about 45% within about 6 hours.

6. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase catalyzes the transfer of a sulfate group to cholecystokinin-8 with a yield of greater than 55% within about 6 hours.

7. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase sulfates a sulfate acceptor selected from the group consisting of a phenolic compound and a tyrosylpeptide.

8. The arylsulfotransferase of claim 7, wherein said sulfate acceptor is a phenolic compound selected from the group consisting of tyrosine, tyrosine methyl ester, tyramine, phenol, catechol, catechin, methyl p-hydroxybenzoate, 4-methylumbelliferone and methyl paraben.

9. The arylsulfotransferase of claim 7, wherein said sulfate acceptor is a tyrosylpeptide selected from the group consisting of cholecystokinin-8, kyotorphin, dermorphin, physalaemin, proctolin, angiotensin I, caerulein, arg8 vasopressin, hirudin(54-65) and leu enkephalin.

10. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase maintains greater than about 60% activity at 4.degree. C. for about 2 weeks without being immobilized or otherwise protected.

11. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase maintains greater than about 80% activity at 4.degree. C. for about 2 weeks without being immobilized or otherwise protected.

12. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase has a donor substrate specificity for p-nitrophenylsulfate as a substrate donor of greater than about 60% activity, wherein 100% activity is measured using p-acetylphenylsulfate as a substrate donor, and wherein tyramine is a sulfate acceptor.

13. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase has a donor substrate specificity for indoxyl sulfate as a substrate donor of greater than about 3% activity, wherein 100% activity is measured using p-acetylphenylsulfate as a substrate donor, and wherein tyramine is a sulfate acceptor.

14. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase does not use 3'-phosphoadenosine-5'-phosphosulfate as a sulfate donor.

15. The arylsulfotransferase of claim 1, wherein said arylsulfotransferase has a donor substrate specificity for estrone sulfate as a substrate donor of greater than about 5% activity, wherein 100% activity is measured using p-acetylphenylsulfate as a substrate donor, and wherein tyramine is a sulfate acceptor.

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Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 20030104001 A1

L9: Entry 1 of 3 File: PGPB Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030104001
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030104001 A1

TITLE: Mycobacterial sulfation pathway proteins and methods of use thereof

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bertozzi, Carolyn R.	Berkeley	CA	US	
Williams, Spencer J.	Berkeley	CA	US	
Mougous, Joseph D.	El Cerrito	CA	US	

US-CL-CURRENT: 424/190.1; 435/193, 435/252.3, 435/320.1, 435/69.3, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6255088 B1

L9: Entry 2 of 3 File: USPT Jul 3, 2001

US-PAT-NO: 6255088
DOCUMENT-IDENTIFIER: US 6255088 B1
**** See image for Certificate of Correction ****

TITLE: Enzymatic sulfation of biomolecules

DATE-ISSUED: July 3, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wong; Chi-Huey	Rancho Santa Fe	CA		
Burkart; Michael D.	Arlington	TX		

US-CL-CURRENT: 435/130; 435/101, 435/193, 435/257.3, 435/320.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6225100 B1

L9: Entry 3 of 3 File: USPT May 1, 2001

US-PAT-NO: 6225100
DOCUMENT-IDENTIFIER: US 6225100 B1
**** See image for Certificate of Correction ****

TITLE: Arylsulfotransferase

DATE-ISSUED: May 1, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Maurina-Brunker; Julie	Appleton	WI		
Grund; Alan D.	Manitowoc	WI		

US-CL-CURRENT: 435/193; 435/183, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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Terms	Documents
3'-phosphoadenosine-5'-phosphosulfate.clm.	3

Display Format: - Change Format

Previous Page Next Page

WEST Search History

DATE: Tuesday, July 15, 2003

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L9	3'-phosphoadenosine-5'-phosphosulfate.clm.	3	L9
L8	3'-phosphoadenosine-5'-phosphosulfate synthetase	0	L8
L7	paps synthetase	6	L7
L6	L2 and paps synthetase	0	L6
L5	gene specific same antibody binding fragment	0	L5
L4	gene specific adj15 antibody binding fragment	0	L4
L3	gene specific adj5 antibody binding fragment	0	L3
L2	gene specific and antibody binding fragment	95	L2
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L1	gene specific antibody binding fragment	0	L1

END OF SEARCH HISTORY

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L10: Entry 1 of 2 File: PGPB Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030104001
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030104001 A1

TITLE: Mycobacterial sulfation pathway proteins and methods of use thereof

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bertozzi, Carolyn R.	Berkeley	CA	US	
Williams, Spencer J.	Berkeley	CA	US	
Mougous, Joseph D.	El Cerrito	CA	US	

US-CL-CURRENT: 424/190.1; 435/193, 435/252.3, 435/320.1, 435/69.3, 536/23.2

CLAIMS:

What is claimed is:

1. An isolated polynucleotide comprising a nucleotide sequence encoding a mycobacterial sulfation pathway polypeptide.

2. The isolated polynucleotide according to claim 1, wherein the sulfation pathway polypeptide is selected from the group consisting of a sulfotransferase, an ATP sulfurylase, an adenylyl phosphosulfate reductase, a 3'-phosphoadenosine-5'-phosphosulfate reductase, an adenylyl phosphosulfate kinase, a sulfatase, and a sulfate transporter.

3. The polynucleotide according to claim 1, wherein said sulfation pathway polypeptide is a sulfotransferase that comprises a motif selected from the group consisting of a 5'-phosphosulfate binding loop, a 3'-phosphate binding motif, and a conserved RYEDL motif.

4. The polynucleotide according to claim 1, wherein said sulfation pathway polypeptide is a sulfotransferase having an amino acid sequence as set forth in any one of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 13, 15, 17, 18, 19, 21, 23, and 25.

5. The polynucleotide according to claim 1, wherein said sulfation pathway polypeptide is an APS reductase having an amino acid sequence as set forth in any one of SEQ ID NOs: 27, 28, and 29.

6. The polynucleotide according to claim 1, wherein said sulfation pathway polypeptide is an APS kinase having an amino acid sequence as set forth in one or SEQ ID NOs:31 and 32.

7. A recombinant vector comprising a polynucleotide according to claim 1.

8. A host cell comprising a recombinant vector according to claim 7.

9. An isolated mycobacterial sulfation pathway polypeptide.

10. The isolated polypeptide according to claim 9, wherein the sulfation pathway polypeptide is selected from the group consisting of a sulfotransferase, and ATP sulfurylase, an adenylyl phosphosulfate reductase, a 3'-phosphoadenosine-5'-phosphosulfate reductase, an adenylyl phosphosulfate kinase, a sulfatase, and a sulfate transporter.

11. The isolated polypeptide according to claim 9, wherein said sulfation pathway polypeptide is a sulfotransferase that comprises a motif selected from the group consisting of a 5'-phosphosulfate binding loop, a 3'-phosphate binding motif, and a conserved RYEDL motif.

12. A genetically modified mycobacterium, wherein said genetically modified mycobacterium comprises a modified sulfation pathway gene, such that said sulfation pathway gene does not direct expression of a sulfation pathway polypeptide, wherein said genetically modified mycobacterium is avirulent.

13. An immunogenic composition comprising a genetically modified mycobacterium according to claim 12; and a buffer.

14. A pharmaceutical composition comprising a genetically modified mycobacterium according to claim 12; and a pharmaceutically acceptable excipient.

15. An in vitro cell-free method of identifying an agent that reduces an activity of a mycobacterial sulfation pathway polypeptide, the method comprising: a) contacting a mycobacterial sulfation pathway polypeptide with a test agent; and b) determining the effect, if any, of the test agent on an activity of the sulfation pathway polypeptide.

16. The method according to claim 15, wherein said mycobacterial sulfation pathway polypeptide is a sulfotransferase, and wherein said determining step comprises: i) combining said sulfotransferase with a labeled sulfate donor and an acceptor molecule; and ii) determining the amount of labeled sulfate transferred from the donor to the acceptor molecule, wherein a reduction in the amount of labeled sulfate in the acceptor molecule, compared to a control in the absence of the test agent, indicates that the test agent reduces activity of the sulfotransferase.

17. An agent identified by the method according to claim 16.

18. The agent according to claim 16, wherein said agent reduces viability and/or virulence of a mycobacterium.

19. A method of treating a mycobacterial infection in a mammal, comprising administering to the mammal a therapeutically effective amount of an agent that reduces an activity of a mycobacterial sulfation pathway polypeptide.

20. The method according to claim 19, wherein the mycobacterial infection is Mycobacterium tuberculosis.

21. A method of reducing the viability of a mycobacterium, comprising contacting the mycobacterium with an agent that reduces an activity of a mycobacterial sulfation pathway polypeptide.

22. A method of reducing virulence of a mycobacterium, comprising contacting the mycobacterium with an agent that reduces an activity of a mycobacterial sulfation pathway polypeptide.

23. A method of increasing an immune response to a pathogenic mycobacterium in a host, comprising administering to the host an immunogenic composition according to claim 13.

24. An in vitro method for identifying an agent that inhibits an activity of a mycobacterial sulfation pathway enzyme, the method comprising: a) culturing a first and a second bacterial cell in separate cultures in the presence of a test agent, wherein the first bacterial cell and the second bacterial cell contain a defect in the sulfation pathway enzyme, and wherein the second bacterial cell is transfected with a polynucleotide comprising a nucleotide sequence that encodes and expresses a mycobacterial sulfation pathway enzyme that complements the defect in the sulfation

pathway enzyme; and b) comparing the growth of the first bacterial culture with the growth of the second bacterial culture, wherein a reduction of growth in the second bacterial culture relative to the first bacterial culture indicates that the agent specifically inhibits the mycobacterial sulfation pathway enzyme.

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L10: Entry 2 of 2 File: USPT Jul 6, 1999

US-PAT-NO: 5919673
DOCUMENT-IDENTIFIER: US 5919673 A

TITLE: One-pot enzymatic sulfation process using 3'-phosphoadenosine-5'-phosphosulfate and recycled phosphorylated adenosine intermediates

DATE-ISSUED: July 6, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wong; Chi-Huey	Rancho Sante Fe	CA		
Lin; Chun-Hung	San Diego	CA		
Shen; Gwo-Jenn	Carlsbad	CA		

US-CL-CURRENT: 435/130; 435/101, 435/52, 435/92

CLAIMS:

We claim:

1. A process for using 3'-phosphoadenine-5'-phosphosulfate (PAPS) in an enzyme-catalyzed sulfation of an acceptor with recycling of phosphorylated adenosine intermediates that comprises the steps of:

(a) admixing the following ingredients in an aqueous medium containing magnesium and potassium ions within a single vessel to form an aqueous reaction medium

(i) 3'-nucleotidase or 3'(2'),5'-bisphosphate nucleotidase;

(ii) ATP sulfurylase;

(iii) APS kinase;

(iv) pyrophosphorylase;

(v) a sulfotransferase;

(vi) at least one adenine-containing compound selected from the group consisting of ATP, ADP, AMP, APS, PAPS and PAP;

(vii) sulfate ion;

(viii) an ATP-regenerating system comprising a phosphate donor and a phosphorylating enzyme; and

(ix) a sulfate acceptor for said sulfotransferase

the concentration of said sulfate ion being greater than the concentration of all of said adenine-containing compound, and the activity of said 3'-nucleotidase being less than that of the enzymes of (ii)-(v); and

maintaining said aqueous reaction medium at a pH value of about 5 to about 10 at a temperature of about zero degrees C to about 40.degree. C. for a time period sufficient for said acceptor to be sulfated.

2. The process according to claim 1 including the further step of recovering the sulfated acceptor.

3. The process according to claim 1 wherein said ATP-regenerating system comprises myokinase, pyruvate kinase and phospho(enol)pyruvate.

4. The process according to claim 1 wherein said sulfotransferase is chondroitin transferase.

5. The process according to claim 1 wherein said sulfotransferase is hydroxysteroid sulfotransferase.

6. The process according to claim 1 wherein said sulfotransferase is NodH sulfotransferase.

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Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 20030104001 A1

L10: Entry 1 of 2 File: PGPB Jun 5, 2003

PGPUB-DOCUMENT-NUMBER: 20030104001
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030104001 A1

TITLE: Mycobacterial sulfation pathway proteins and methods of use thereof

PUBLICATION-DATE: June 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bertozzi, Carolyn R.	Berkeley	CA	US	
Williams, Spencer J.	Berkeley	CA	US	
Mougous, Joseph D.	El Cerrito	CA	US	

US-CL-CURRENT: 424/190.1; 435/193, 435/252.3, 435/320.1, 435/69.3, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 2. Document ID: US 5919673 A

L10: Entry 2 of 2 File: USPT Jul 6, 1999

US-PAT-NO: 5919673
DOCUMENT-IDENTIFIER: US 5919673 A

TITLE: One-pot enzymatic sulfation process using 3'-phosphoadenosine-5'-phosphosulfate and recycled phosphorylated adenosine intermediates

DATE-ISSUED: July 6, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wong; Chi-Huey	Rancho Sante Fe	CA		
Lin; Chun-Hung	San Diego	CA		
Shen; Gwo-Jenn	Carlsbad	CA		

US-CL-CURRENT: 435/130; 435/101, 435/52, 435/92

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Terms	Documents
atp sulfurylase and aps kinase.clm.	2

Display Format: - Change Format

Previous Page Next Page

WEST Search History

DATE: Tuesday, July 15, 2003

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L9	3'-phosphoadenosine-5'-phosphosulfate.clm.	3	L9
L8	3'-phosphoadenosine-5'-phosphosulfate synthetase	0	L8
L7	paps synthetase	6	L7
L6	L2 and paps synthetase	0	L6
L5	gene specific same antibody binding fragment	0	L5
L4	gene specific adj15 antibody binding fragment	0	L4
L3	gene specific adj5 antibody binding fragment	0	L3
L2	gene specific and antibody binding fragment	95	L2
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L1	gene specific antibody binding fragment	0	L1

END OF SEARCH HISTORY